Blend for 3 to 5 minutes. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *Dissolution.* Proceed as directed in § 436.215 of this chapter, except:

(i) In lieu of paragraph (a) of that section, a distance of 4.5±0.5 centimeters should be maintained between the lower edge of the stirring blade and the lowest inner surface of the vessel during the test; and

(ii) In lieu of paragraph (d) of that section, use the interpretation described in the United States Pharmacopeia XX dissolution test. The quantity, *Q* (the amount of doxycycline dissolved) is 55 percent at 60 minutes and 85 percent at 90 minutes.

(4) *Identity.* Proceed as directed in § 436.308 of this chapter, except prepare the sample and standard solutions as follows: Grind tablet to a powder. Dissolve precise amount of the doxycycline tablet and of the doxycycline working standard in methanol and further dilute each solution to a concentration of 1 milligram of doxycycline per milliliter. Prepare the sample-standard mixed solution by mixing equal volumes of the final standard and sample solutions. The standard and sample must each produce a major, yellow fluorescent spot with the same R_f value and the standard-sample mixed solution must show no separation of major spots.

[46 FR 7273, Jan. 23, 1981, as amended at 48 FR 23813, May 27, 1983; 48 FR 51293, Nov. 8, 1983; 50 FR 19920, May 13, 1985]

§ 446.120d Doxycycline hyclate pellet-filled capsules.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Doxycycline hyclate pellet-filled capsules contain pellets which are composed of doxycycline hyclate and suitable and harmless diluents, binders, and lubricants. Each capsule contains doxycycline hyclate equivalent to 100 milligrams of doxycycline. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of doxycycline that it is represented to contain. The moisture content is not more than 5.0 percent. It passes the acid resistance test. It passes the dissolution test. The doxycycline hyclate conforms to the standards prescribed by § 446.20(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The doxycycline hyclate used in making the batch for potency, safety, moisture, pH, doxycycline content, identity, and crystallinity.

(*b*) The batch for potency, moisture, acid resistance, and dissolution.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(*a*) The doxycycline hyclate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of 100 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place a representative number of capsules into a high-speed glass blender jar containing 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of doxycycline per milliliter (estimated). Blend for 3 to 5 minutes. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.100 microgram of doxycycline per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *Acid resistance.* Proceed as directed in § 436.543 of this chapter.

(4) *Dissolution.* Empty the contents of one pellet-filled capsule into the basket and proceed as directed in § 436.544 of this chapter. The quantity *Q* (the amount of doxycycline dissolved) is 85 percent at 30 minutes.

[50 FR 41679, Oct. 15, 1985, as amended at 55 FR 11584, Mar. 29, 1990]